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# Quality of life in patients with chronic heart failure and their carers: a 3-year follow-up study assessing hospitalization and mortality

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## Aims

Chronic heart failure (CHF) due to left ventricular systolic dysfunction is associated with poor quality of life (QoL). This study aimed to assess factors affecting health-related QoL in CHF patients and their carers and the impact of QoL on clinical outcomes.

## Methods and results

Demographic, social, and clinical data were collected for consecutive CHF patients in an academic hospital setting. All patients ( $n = 179$ ) and informal carers ( $n = 131$ ) completed a generic QoL questionnaire (EQ-5D) and patients also completed a CHF-specific QoL questionnaire (Minnesota Living with Heart Failure Questionnaire, MLHFQ). Patients were then followed up for 3 years to assess subsequent hospitalizations and mortality. Minnesota Living with Heart Failure Questionnaire score was independently predicted by NYHA class, socioeconomic deprivation and lack of an informal carer. Severity of heart failure, anaemia, and cancer co-morbidity in CHF patients were associated with poor QoL in carers. Chronic heart failure patients with poor baseline QoL (MLHFQ > median) were at increased risk of hospital admissions [hazard ratios (HR) 7.3,  $P < 0.001$ ] and death (HR 1.5,  $P = 0.09$ ). Mortality was also independently associated with repeat hospitalization (HR 6.0,  $P < 0.001$ ) and lack of beta-blocker therapy (HR 1.8,  $P = 0.03$ ).

## Conclusion

Severe heart failure, poor socioeconomic status and lack of social support results in poor QoL in CHF patients which in turn leads to an increased risk of hospital admissions and death. Quality of life in carers is lower in female carers, those with socioeconomic deprivation and those caring for patients with higher NYHA class or having a cancer. Quality of life assessment may complement clinical prognostic markers to identify CHF patients at high risk of adverse events.

## Keywords

Heart failure • Quality of life • Prognosis • Hospitalization • Mortality

## Introduction

Chronic heart failure (CHF) due to left ventricular systolic dysfunction (LVSD) is associated with significant morbidity and in advanced stages has a mortality worse than many cancers.<sup>1</sup> A recent report has demonstrated that widespread use of evidence-based drugs and devices over the last 10 years has resulted in significant improvements in survival in CHF patients.<sup>2</sup> Although improving survival remains clinically important, many patients with advanced heart failure give equal or more importance to quality of life (QoL) when compared with length of life.<sup>3</sup> Quality of life in patients with heart failure is not only significantly

reduced when compared with the general population, but CHF also causes more severe impairment of physical and psychosocial functioning than other chronic diseases such as chronic airway disease, arthritis and ischaemic heart disease.<sup>4</sup> Quality of life, symptom burden and emotional well-being in CHF patients is indeed as poor as in patients with cancer.<sup>5</sup> Improving QoL is increasingly being recognized as a major aim of treatment in clinical practice and as an outcome measure in clinical trials.<sup>6</sup> Previous studies exploring factors affecting QoL have focused mainly on clinical variables, overlooking the impact of psychosocial variables, potential interaction of clinical and non-clinical variables and interaction of QoL in patients and carers.<sup>7</sup> The effect of QoL on

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subsequent CHF-related adverse events has previously been reported in the literature.<sup>6,8–11</sup> However, these studies often included selected subgroups of CHF patients, were performed on sub-sets within clinical trials or had relatively short follow-up. This study aimed to explore the effects of a wide range of clinical, social, psychological, and demographic factors on QoL in an unselected cohort of CHF patients and their informal carers and to investigate the impact of baseline QoL on hospitalization and mortality over a 3-year follow-up period.

## Methods

The study was approved by Lothian Research Ethics Committee and conforms to the principles outlined in the Declaration of Helsinki. All subjects gave written informed consent to participate.

### Study participants

Consecutive patients with CHF ( $n = 179$ ), diagnosed clinically using Framingham criteria and confirmed to have LVSD on echocardiography, were identified either from cardiology wards at time of discharge ( $n = 101$ ) or outpatient clinics ( $n = 78$ ). Demographic, social, and clinical data were collected for all the patients from computerized hospital and primary care records. Where the patient identified a specific informal carer, a family member or a close friend, these individuals ( $n = 131$ ) were also asked to complete a QoL questionnaire and their basic demographic details (age, gender, and postcode) were documented. Socioeconomic status was derived from the patients and carers postcode (zipcode) using the Scottish Index of Multiple Deprivation (SIMD) which provides a numeric score, ranging from 0.54 (least deprived) to 87.6 (most deprived), based on a national census examining employment status, education and skills, housing, average income, and access to services.<sup>12</sup>

### Quality of life assessment

Quality of life was assessed using European QoL-5 Dimensions (EQ-5D) and Minnesota Living with Heart Failure Questionnaire (MLHFQ). European QoL-5 Dimensions is a standardized instrument to provide a single-index value for health-related QoL and has been validated in general population and heart failure patients.<sup>13</sup> Minnesota Living with Heart Failure Questionnaire has been widely used and validated to assess QoL in CHF patients and to explore effect of different interventions. All patients completed both EQ-5D and MLHFQ, at least 1 month after discharge or at the time of attendance at an outpatient clinic. The informal carers completed EQ-5D questionnaire at baseline. Questionnaires were sent to patients and carers by post and were followed up by a single phone call if no response was received within 2 weeks.

### Follow-up

Mean follow-up period in this study was 40 months (range 33–45). Total number of hospital admissions and CHF-related hospital admissions during follow-up were assessed using hospital records and local computerized patient administration system. All-cause mortality was assessed using the national Central Health Index database.

### Statistical analyses

Data are presented as Mean  $\pm$  SEM or as percentages (proportions) unless stated otherwise. Analysis was carried by using student's *t*-test or one-way ANOVA for parametric data, Mann–Whitney U-test for non-parametric data and  $\chi^2$  or Fisher's exact test for categorical

data. Variables with significant trend ( $P < 0.1$ ) were entered in multiple regression analysis models to determine the influence of variables on QoL and CHF-related hospital admissions. For mortality analysis, Cox proportional-hazards regression survival model was used. The hazard ratios (HR) with confidence interval (CI) and *P* values are presented. For parameters demonstrating significance in the multivariate analysis, survival curves were computed using the Kaplan–Meier method. All statistical analyses were performed using SPSS for windows version 17.0 (SPSS Inc., Chicago, USA).

## Results

### Patient characteristics

The overall study cohort included 179 patients and 131 informal carers. The mean age was 71 years for CHF patients and 63 years for carers. Seventy-two per cent of the patients and 16% of carers were males. Nearly two-thirds (62%,  $n = 110$ ) of CHF patients had ischaemic heart failure. The remainder (38% patients with non-ischaemic aetiology) had hypertension (13%), valvular heart disease (9%), alcoholic cardiomyopathy (5%), and idiopathic dilated cardiomyopathy (10%). The baseline clinical, social, and demographic characteristics for all participants are described in Table 1.

### Quality of life in chronic heart failure patients

Chronic heart failure patients had poor QoL with a mean QoL score of  $50 \pm 2$  on MLHFQ and  $0.57 \pm 0.03$  on EQ-5D questionnaire. There was a strong correlation between the EQ-5D and MLHFQ scores (Spearman correlation coefficient  $-0.75$ , CI  $-0.67$  to  $-0.81$ ,  $P \leq 0.001$ ).

Chronic heart failure patients with poor QoL were younger, predominantly male, with lower socioeconomic status, higher NYHA class, more likely to have chronic airway disease and less likely to be taking beta-blocker drug therapy (Table 1).

Variables with a test of significance at  $P < 0.1$  by univariate analysis were entered into a multiple regression model. After adjustment for all variables, lower QoL (higher MLHFQ score) in CHF patients was independently associated with more severe heart failure symptoms (NYHA class), lower socioeconomic status (SIMD score) and not having an informal carer (Table 2).

### Quality of life in carers

Quality of life of carers was better than CHF patients (EQ-5D  $0.76 \pm 0.02$  vs.  $0.57 \pm 0.03$ ,  $P = 0.02$ ). Quality of life of carers also correlated with QoL of patients; people caring for CHF patients with poor QoL had lower QoL scores than carers of patients with good QoL ( $0.72 \pm 0.01$  vs.  $0.83 \pm 0.01$ ,  $P = 0.01$ ). Quality of life was particularly low in female carers compared with male carers ( $0.74 \pm 0.02$  vs.  $0.86 \pm 0.05$ ,  $P = 0.03$ ). Moreover, carer QoL was also affected by patient-related factors including severity of heart failure symptoms, presence of anaemia or a cancer. Multiple regression analysis demonstrated that carers QoL was independently associated with carer's sex, carer deprivation (SIMD score), patient NYHA class, and patient co-morbidity with a cancer (Table 2).

**Table 1** Baseline characteristics of patients and carers

Variables	Entire group	QoL groups		
		MLHFQ < Median (Good QoL)	MLHFQ > Median (Poor QoL)	P <sup>‡</sup>
Patients				
Demographic and Social				
Age (years)	71 ± 1	73 ± 1	69 ± 2	0.02
Male (%)	72	64	81	0.01
SIMD score	17.0 ± 1.1	12.2 ± 1.2	21.9 ± 1.6	<0.001
Home owner (%)	47	50	44	ns
Institutional care (%)	2.3	2.2	2.4	ns
Pts. having a carer (%)	72	82	69	0.09
Pts. living with carer (%)	48	51	45	ns
Clinical profile				
LVSD				
Mild (%)	30	33	25	ns
Moderate (%)	42	40	45	ns
Severe (%)	28	28	30	ns
NYHA				
I and II (%)	59	78	39	<0.001
III and IV (%)	41	22	61	<0.001
CHF aetiology				
Ischaemic (%)	62	62	61	ns
Non-ischaemic (%)	38	38	39	ns
Creatinine (μmol/L)	121 ± 3	116 ± 4	124 ± 4	ns
Haemoglobin (g/dL)	131 ± 2	131 ± 1	130 ± 2	ns
Duration of CHF (m)	27.7 ± 3	29.7 ± 4	25.5 ± 4	ns
Co-morbidities (%)				
Chronic obstructive pulmonary disease	8.5	4.4	12.6	0.05
Diabetes	29	24	34	0.09
Hypertension	44	44	44	ns
Arthritis	9.6	6.6	12.6	ns
Cancer	8	10	6	ns
Stroke	6.8	6.7	6.9	ns
Depression	5.1	4.4	5.7	ns
Medication (%)				
Beta-blockers	56	66	45	0.003
Diuretics	93	94	92	ns
ACE Inhibitors	71	72	70	ns
Spironolactone	33	12	21	0.03
Statins	55	51	59	ns
Digoxin	46	42	51	ns
Carer characteristics				
Age (years)	63 ± 1	63 ± 1	63 ± 2	ns
Male (%)	16	21	6	0.02
SIMD score	16.3 ± 1.8	13.8 ± 1.7	18.8 ± 2.0	0.05
EQ-5D score	0.76 ± 0.03	0.83 ± 0.0	0.72 ± 0.0	0.01
Daily visit to patient (%)	57	53	62	ns
Full time job (%)	31	43	13	0.001

SIMD, Scottish Index of Multiple Deprivation; LVSD, Left Ventricular Systolic Dysfunction; MLHFQ, Minnesota Living with Heart Failure Questionnaire; ns, non-significant.

\*P-value was calculated using student's t-test/Mann-Whitney U-test for continuous data and  $\chi^2$  test/Fisher's exact test for categorical data.

## Effect of quality of life and other variables on mortality

During the follow-up period of 3 years (average 40 months), 67 patients (37%) died. There were significantly more deaths in patients with poor QoL (MLHFQ > median) when compared with patients with higher QoL score at baseline (46 vs. 31%,  $P = 0.03$ ). Patients in the lowest baseline MLHFQ QoL quartile (Q4) had a worse prognosis than other groups (HR 1.7, CI 1.1–2.9,  $P = 0.03$ , Figure 1A). Other factors associated with survival using univariate analysis were age, CHF-related hospital admissions, NYHA class, lack of beta-blocker and lack of ACE inhibitor therapy, haemoglobin and creatinine levels, and co-morbidity with cancer (Table 3).

**Table 2** Factors independently associated with quality of life in chronic heart failure patients and carers

QoL (MLHFQ score) in CHF patients		QoL (EQ-5D score) in carers	
Variable	$P^*$	Variable	$P^*$
NYHA class	<0.001	NYHA class of patient	0.02
SIMD score	0.002	Caring patient with a cancer	0.01
Patient without informal carer	0.01	Carer's gender	0.03
		Carer's SIMD score	0.04

SIMD, Scottish Index of Multiple Deprivation; MLHFQ, Minnesota Living with Heart Failure Questionnaire.

\* $P$ -value from multiple regression analysis.

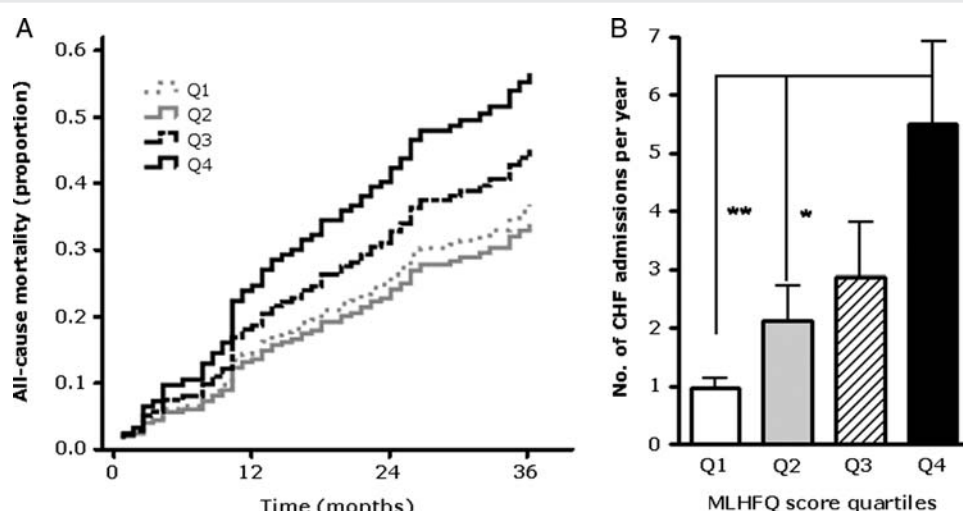
Using Cox proportional hazards model, CHF-related hospital admissions (HR 6.0, CI 3.3–10.0,  $P < 0.001$ ) and lack of beta-blocker therapy (HR 1.8, CI 1.1–2.8,  $P = 0.03$ ) emerged as independent factors affecting survival whereas presence of cancer co-morbidity (HR 1.5, CI 0.9–2.8,  $P = 0.07$ ) and poor QoL (HR 1.5, CI 0.9–2.9,  $P = 0.1$ ) demonstrated a trend (Figure 2).

## Effect of quality of life and other variables on hospital admissions

Hospital admissions were significantly greater in patients with poor base-line QoL when compared with better QoL group (No. of CHF admissions:  $4.8 \pm 0.8$  vs.  $1.5 \pm 0.3$ ,  $P = 0.004$ ). Detailed analysis by comparison of QoL quartiles showed a significant step-wise increase in number of CHF-related hospital admissions with worsening QoL at baseline (Figure 1B). Other factors associated with hospital admission by univariate analysis, included NYHA class ( $P < 0.001$ ), age ( $P < 0.001$ ), MLHFQ score ( $P < 0.001$ ), duration of CHF ( $P < 0.001$ ), use of ACE inhibitors ( $P < 0.01$ ) and beta-blockers ( $P < 0.01$ ), creatinine level ( $P < 0.01$ ), depression ( $P < 0.05$ ), gender ( $P = 0.05$ ), haemoglobin level ( $P = 0.05$ ), and co-morbidity with diabetes ( $P = 0.05$ ). These factors were included in multiple regression analyses to identify independent variables affecting total (all-cause) and CHF-related hospital admissions and results are summarized in Table 4.

## Discussion

This study provides a contemporary and comprehensive evaluation of the influence of clinical, social, and socioeconomic variables on QoL in CHF patients and their informal carers. The findings highlight the association between QoL, recurrent hospitalization and mortality in CHF patients.



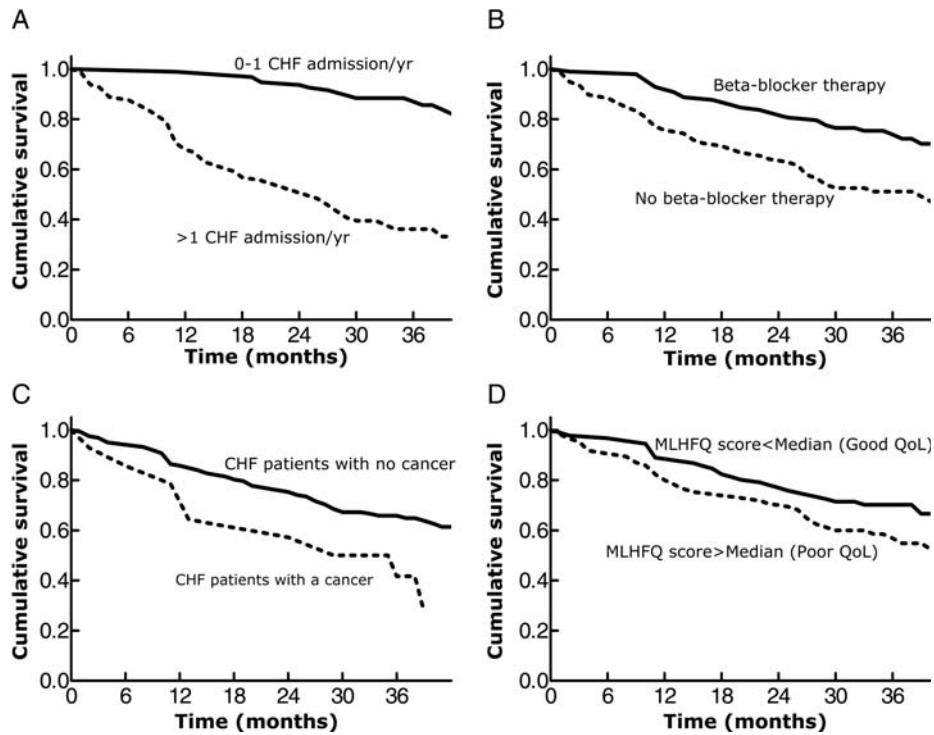
**Figure 1** Baseline quality of life predicts mortality and hospital admissions. Chronic heart failure patients in worst quality of life (MLHFQ score) quartile (Q4) had significantly higher mortality ( $P = 0.03$ ) in 3-year follow-up period (A). MLHF quartiles also correlate significantly with chronic heart failure-related hospital admissions (B). One-way ANOVA showed a significant difference between the four groups ( $P < 0.01$ ). Post hoc analysis with Tukey's multiple comparison test showed significant difference between Q1 and Q4 ( $P < 0.01$ ) and also between Q2 and Q4 ( $P < 0.05$ ).

**Table 3** Variables affecting survival in chronic heart failure patients (Kaplan–Meier univariate analysis)

Variables	Groups	Survival (months)	P
CHF hospitalization	0–1 CHF admission per year	44.3	<0.001
	> 1 CHF admission per year	26.7	
Beta-blockers	Patients receiving drug	39.7	0.001
	Patients NOT receiving drug	31.8	
NYHA class	Class I and II	39.5	0.002
	Class III and IV	31.3	
Cancer	Patient without cancer	36.9	0.003
	Patient with cancer	28.1	
Creatinine (μmol/L)	Less than 130 (median)	38.4	0.03
	More than 130 (median)	33.3	
MLHFQ Score	Score less than 50 (median)	38.5	0.04
	Score more than 50 (median)	33.9	
ACE Inhibitors	Patients receiving drug	38.0	0.04
	Patients NOT receiving drug	30.9	
Haemoglobin (g/dL)	More than 120 (median)	38.4	0.08
	Less than 120 (median)	33.8	
Age (years)	Less than 70 (median)	37.5	0.09
	More than 70 (median)	33.3	

**Factors affecting quality of life in chronic heart failure patients and carers**

NYHA class, socioeconomic deprivation (SIMD score) and presence of an informal carer emerged as three independent predictors of QoL in CHF patients, after adjustment for confounding variables. NYHA class has been shown to correlate well with QoL in a number of studies.<sup>7,14</sup> However, there are few studies that have examined socioeconomic deprivation using a validated tool and only one that found an association with current or former occupational status.<sup>15</sup> Our study, using a tool for multiple measures of deprivation, provides stronger evidence for this association. Our study also indicated that patients who did not have an informal carer had a worse QoL than those who could identify a carer. It has been shown previously that QoL in CHF patients having a marital relationship is better than the CHF patients living alone<sup>16</sup> and also the changes in social support can influence health-related QoL.<sup>17</sup> Our findings, therefore, further highlight the importance of home-support for CHF patients. The effect of age on QoL in heart failure patients is not as clear as in the general population where increasing age leads to progressive reduction in QoL. Some studies have reported worsening QoL with age<sup>15</sup> and other studies have reported opposing results.<sup>14</sup> Our data suggest that younger CHF patients have worse QoL than older patients but this association was not strong and became non-significant after adjustment for other variables.



**Figure 2** Kaplan–Meier survival curves. Survival in chronic heart failure patients was associated with number of chronic heart failure-related hospital admissions (A), usage of beta-blockers (B), co-morbidity with any cancer in chronic heart failure patients (C) and baseline quality of life (D).



**Table 4** Factors independently associated with hospitalization in chronic heart failure patients

Variable	CHF admissions*	Total admissions*
QoL score	<0.0001	0.02
Beta-blockers usage	0.04	ns
NYHA	ns	0.01
ACE Inhibitors usage	ns	0.01
Chronic obstructive pulmonary disease	ns	0.03
Age	ns	0.04

ns, non-significant P-value.

\*P values from multiple regression analyses.

Quality of life in carers, assessed by EQ-5D, was slightly lower than expected in the general population.<sup>18</sup> Female carers demonstrated overall poorer QoL than male carers which is consistent with previous observations in partners of CHF patients.<sup>19</sup> The underlying cause of this gender difference remains uncertain and merits further study. An association between QoL in patients and carers has been observed in studies of cancer patients.<sup>20</sup> In our study, although the QoL scores in patients were closely associated with QoL scores in their informal carers, after statistical adjustment for confounding factors this association was no longer significant. One might expect some link between carers QoL and patients hospital admissions, however, we did not find an association between carers QoL and CHF-related events in patients. On the other hand, severity of heart failure, presence of anaemia, and co-morbidity with a cancer in CHF patients were found to be independently linked to QoL of carers.

## Factors affecting hospitalization and mortality

Heart failure is a leading cause of hospital admission, particularly in elderly patients, placing a significant burden on health care resources. This longitudinal study suggests that CHF hospitalization is a strong independent predictor of mortality. This important finding reinforces the findings of other studies<sup>21–23</sup> and highlights the need for greater emphasis on interventions that reduce hospitalizations. Our findings also potentially support the use of using heart failure hospital admissions as a marker in identifying patients who may be reaching end of life.<sup>24</sup>

Cancer co-morbidity was independently associated with mortality in our study population. There were only 14 patients with the combined diagnosis of CHF and a malignancy but it is clear that this group merits special attention in the clinical setting with early consideration for extra supportive care regardless of the perceived clinical prognosis.

The finding that lack of use of beta-blocker drugs was linked to both mortality and hospitalization underscores the significant benefits that are lost in CHF patients with LVSD not treated with beta-blockers and is consistent with previous literature.<sup>25</sup> Chronic heart failure patients in our study were managed within a specialized

cardiology service either by a multidisciplinary team led by specialist nurses or in a consultant-led cardiology outpatient setting. Therefore, although the overall use of beta-blockers appears low, it is likely that this was due to co-morbidities or intolerance. In support of this, patients not on beta-blockers were older, had significantly more chronic obstructive pulmonary disease, anaemia, low blood pressure, and renal impairment (data not shown). It is likely that a combination of the absence of beta-blockers (and their attendant benefits) and the presence of these co-morbidities confer poorer outcome.

## Clinical implications

The Advanced Heart Failure Study Group of the European Society of Cardiology has recently stressed the need for promoting the development of heart failure oriented palliative care services across Europe.<sup>26</sup> However, it is well acknowledged that identification of CHF patients approaching end of life and in need of palliative care can be extremely difficult.<sup>5,26</sup> One approach is to use clinical prognostic models based on patient cohorts from acute<sup>27–29</sup> and ambulant<sup>23,30,31</sup> CHF populations. Whereas helpful, these models have major limitations in that they primarily focus on clinical factors, they are based on assessment of prognosis in populations and not individual patients,<sup>32</sup> and some are based on datasets derived from randomized controlled trials.<sup>23,28</sup> The UK national Gold Standards Framework (GSF) includes NYHA class (III and IV) and repeated hospitalization as tools to identify patients at end of life due to CHF<sup>24</sup> and these factors were also identified as important in our study. Our study suggests that QoL assessed by MLHFQ may complement clinical markers of poor prognosis. Formal measurement of QoL as a routine part of clinical assessment may not only identify patients with a poor composite QoL score but may also allow the care provider to address-specific QoL domains in a way that is of benefit to the individual patient. Serial assessment of QoL may also provide additional valuable information regarding disease progression, response to interventions and prognosis and merits further study.

## Study limitations

This study has several potential limitations. The number of patients and carers enrolled in this study is relatively small; however, we analysed a large number of variables covering clinical and social characteristics not included in previous studies. Furthermore, our study included unselected patients from routine clinical settings with follow-up for 3 years. This makes our finding more relevant to real life clinical practice. Further possible limitations of our study include lack of data on biochemical markers of CHF including brain natriuretic peptide (BNP) which has been shown to have association with CHF outcome.<sup>14</sup> However, BNP was not available in our centre at the time of this study. We only included patients with LV systolic dysfunction, so results may not be applicable to heart failure patients with preserved systolic function and additional studies may be needed to address this issue.

## Conclusion

In conclusion, this study indicates that higher NYHA class, poor socioeconomic status and lack of informal carer results in poor QoL in CHF patients. Quality of life in carers is lower in female

carers, those with socioeconomic deprivation and those caring for patients with higher NYHA class or having a cancer. Poor QoL in patients predicts an increased risk of CHF-related and all-cause hospital admissions. Repeated hospitalization, lack of use of beta-blockers, co-morbidity with a cancer, and poor QoL are associated with higher mortality in CHF patients. Patient assessment protocols for CHF should combine clinical prognostic factors and self-reported QoL scoring to identify those at risk of recurrent hospitalization and death.

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**Conflict of interests:** none declared.

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